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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,809	06/30/2000	GEORGE E. SEIDEL	XY-LODO-USNP	3161
33549 7590 02/27/2009 SANTANGELO LAW OFFICES, P.C. 125 SOUTH HOWES, THIRD FLOOR FORT COLLINS, CO 80521				
EXAMINER				
MYERS, CARLA J				
ART UNIT		PAPER NUMBER		
1634				
NOTIFICATION DATE		DELIVERY MODE		
02/27/2009		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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# Office Action Summary

Application No.

09/582,809

Applicant(s)

SEIDEL ET AL.

Examiner

Carla Myers

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2009.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 221, 222, 224, 225 and 227 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 221, 222, 224, 225 and 227 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

#### DETAILED ACTION

##### Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 19, 2009 has been entered.

2. Applicant's arguments and amendments set forth in the response of January 19, 2009 have been fully considered but are not persuasive to place all claims in condition for allowance. All rejections not reiterated herein are hereby withdrawn. In particular, the prior rejection of claims 221-227 under 35 USC 112, first paragraph (new matter) as it pertained to the recitations of "no more than about 350,000," "no more than about 5 hours," "no more than about 6 hours," and "at least 5 degrees Celsius" has been obviated by the amendments to the claims. The previous rejections of the claims under 35 USC 103 are withdrawn in favor of the following new grounds of rejection.

3. Claims 221, 222, 224, 225 and 227 are pending and have been examined herein. This action is made final.

##### Terminal Disclaimer

4. The terminal disclaimer filed on January 19, 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of

any patent that issues from U.S. Application No. 11/536,492 has been reviewed and is accepted. The terminal disclaimer has been recorded.

### New Grounds of Rejection

#### Claim Rejections - 35 USC § 112 second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 221, 222, 224, 225 and 227 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 221, 222, 224, 225 and 227 are indefinite over the recitation of "about an equal number of sperm cells" because the claims do not set forth what the equal number of sperm cells is being compared to. For example, it is unclear as to whether the equal number of sperm cells is in comparison to the artificial insemination sample having no more than 300,000 sorted sperm cells, or to any unsorted artificial insemination sample, or to the originally collected sperm sample, or the originally sorted sperm sample. It is also unclear as to what is intended to be encompassed by statistically comparable levels between fertilizing at least one egg in a female bovine and an unsorted artificial insemination sample per se. While it is clear as to what is encompassed, for example, by fertilization success levels obtained with an artificial insemination sample having 300,000 sorted sperm cells being statistically comparable to fertilization success levels obtained with an artificial insemination sample having 300,000 unsorted sperm cells, it is unclear as to what is intended to be encompassed

Art Unit: 1634

by comparing the success levels of fertilization to unsorted artificial insemination sample per se (i.e., versus the success levels obtained with the unsorted artificial insemination sample).

### Maintained Rejections

#### Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 221, 222, 224, 225 and 227 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the recitation in the claims of "fertilizing at least one egg within said female bovine at success levels statistically comparable to an unsorted artificial insemination sample having about an equal number of sperm cells." There does not appear to be support in the specification as originally filed for the concept a method of artificial insemination wherein fertilization with an artificial insemination sample having no more than 300,000 sex sorted sperm cells results in a statistically comparable success level of fertilization as compared to that achieved using an artificial insemination sample comprising about the same number of unsorted sperm cells.

Further, it is noted that originally filed claim 1 is drawn to a method wherein artificial insemination is performed using a low number of sorted sperm cells relative to a "typical artificial insemination dosage" and fertilization of at least one egg occurs "at success levels statistically comparable to the typical unsexed artificial insemination dosage." In originally filed claim 1, fertilization success levels are expressed as a comparison between a low dosage sorted sperm sample and a "typical" unsorted sperm dosage (e.g. a sample having 10% to 50% or more sperm cells as compared to the low dosage sorted sperm sample). Accordingly, this recitation does not provide support for the distinct concept set forth in the present claims wherein fertilization success levels are expressed as a comparison between the artificial insemination sample having no more than 300,000 of the sex sorted sperm cells and the artificial insemination sample having about an equal number of unsorted sperm cells.

Response to Remarks:

In the response, Applicants point to Example 1 of the specification as providing support for this amendment. Example 1 (page 25) states that "[a]lthough the pregnancy rate with sexed semen was only 80% of controls, this difference was not statistically significant ( $>0.1$ ).". Applicants conclude that from this teaching it is clear that pregnancy rates between the two doses were compared and found to be statistically comparable.

This argument and the cited teachings in the specification have been fully considered but are not persuasive. Example 1 is characterized as achieving a pregnancy rate with sex sorted semen that was 80% of that of controls and as indicating that the 80% of controls pregnancy rate was not statistically different. This concept is

significantly distinct from the concept set forth in the present claims. First, it is noted that the specification does not define how fertilization and pregnancy rates were determined and does not specifically teach that pregnancy rates are considered to be identical to fertilization rates. Pregnancy and fertilization rates do not appear to be identical to one another in the context of Example 1 since pregnancy was not determined ultrasonically under 31-34 days after insemination (see page 25). That is, the actual fertilization rate may have been higher than the pregnancy rate observed at days 31-34 post insemination. Thereby, the teachings regarding a pregnancy rate of 80% of that of controls does not provide support for the concept of particular fertilization rates (e.g., a fertilization rate that is 80% of that of controls). Secondly, the teachings at page 25 of the specification provide support only for the concept of pregnancy rates that are 80% of that of controls, wherein the control is an artificial insemination sample containing  $3 \times 10^5$  liquid (unfrozen) sperm cells. While the 80% pregnancy rate of controls is characterized as not statistically different, this teaching does not provide support for all statistically comparable pregnancy rates (e.g., 81%, 82%, 83% etc) as compared to controls containing about an equal number of sperm cells, only pregnancy rates that are 80% of that obtained using  $3 \times 10^5$  liquid (unfrozen) sperm cells.

#### New/Modified Grounds of Rejection

#### Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

Art Unit: 1634

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 221, 222, 224, 225 and 227 are rejected under 35 U.S.C. 103(a) as being unpatentable Seidel (Theriogenology, January 1996, vol. 45, page 309; cited in the IDS of June 30, 2000) in view of Rens (U.S. Patent No. 5,985,216), as evidenced by the specification (page 25).

Seidel (Jan 1996) teaches methods of bovine artificial insemination comprising collecting sperm cells from a male bovine, sorting the sperm cells according to sex using flow cytometry wherein the sperm cells are sorted at a rate of up to  $2 \times 10^6$  of each sex of sperm/5-6 hours to purity rates of about 90%, concentrating the sorted sperm cells, establishing an artificial insemination sample consisting of  $1-2 \times 10^5$  of sorted sperm cells (i.e., "no more than 300,000" sorted sperm cells) in a .1ml volume, inserting the artificial insemination sample into the uterine horns of the female bovine after the onset of estrus; and fertilizing at least one egg within said female bovine. Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5°C during shipping were pregnant at 8 weeks. Given this 50% pregnancy rate, the method of Seidel is considered to be one that fertilizes eggs within a female bovine at success levels statistically comparable to that achieved using an artificial insemination sample comprising about the same number of unsorted sperm cells. It is noted that the claims



do not particularly define the fertilization levels achieved using artificial insemination samples comprising about an equal number of unsorted sperm cells. However, the specification (page 25, Example 1) teaches that insemination with a sample of 300,000 unsorted sperm cells achieved a pregnancy rate of 54%. Since a 50% pregnancy rate is statistically comparable to a 54% pregnancy rate (i.e., 93%), the method of Seidel which used fewer sperm than the 300,000 unsorted sperm that achieved a 54% pregnancy would necessarily have the property of achieving fertilization rates statistically comparable to that achieved using an unsorted artificial insemination sample having about an equal number of sperm cells. Note that the specification has been cited only to establish what constitutes a fertilization success level achieved with an unsorted artificial insemination sample, and thereby what constitutes a statistically comparable fertilization success level.

Seidel does not teach sorting sperm cells at rates of at least 500 sorts/second.

However, Rens teaches a method of sex-sorting sperm using high speed flow cytometry. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoechst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are collected. Importantly, Rens (col. 5) discloses modifying the MoFlo® high speed cell sorter to include a new elliptical nozzle capable of more accurately

orienting sperm for accurate sorting. Rens teaches use of the modified MoFlo® sorter using sampling rates of 500 sperm/second and 2000 sperm/second (column 6). Further, Rens teaches that the modified MoFlo® sorter also allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens (col. 2) teaches that the flow cytometry apparatus disclosed therein provides for improved accuracy and efficiency of sorting, as compared to prior art flow cytometers. Rens (col. 2) also discloses the motivation to use high speed cell sorters to maximize the number of sorted sperm per unit time. For example, Rens (col. 4) discuss the requirement to use large quantities of sperm for artificial insemination and states that by using the high speed cell sorter equipped with the nozzle disclosed therein, the yield of sex sorted sperm cells can be increased at least 10 fold, making artificial insemination with sexed semen a more feasible option. Rens (col. 7) also exemplifies a method wherein a total of 50 million X and Y sperm were sorted in a 7 hour period using the modified MoFlo® sorter equipped with the new elliptical nozzle.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have used high sorting rates, including sorting rates of at least 500 sorts /second in order to have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Further,

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). In the present situation, the prior art teaches provides the motivation to increase sort speeds to at least 500 sorts/sec and the means for achieving this result (i.e., the modified MoFlo® high speed sorter including the elliptical nozzle of Rens). Thereby, modification of the method of Seidel to use the high speed sorter of Rens to sex-sort sperm cells at rates of 500 sorts/sec would have been obvious to one of ordinary skill in the art and well within the skill of the art at the time the invention was made.

Additionally, as stated in *Ex parte Kubin* (No. 2007-0819, Bd. Pat. App. & Int. May 31, 2007): "Under *KSR*, it is now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation to solve a problem and there are a finite number of identified predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under 103. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct 1727, 82 USPQ2d 1385, 1397 (2007)." This reasoning is also applicable to the present situation wherein the prior art of Rens provides both the

motivation to increase the rate of sorting and collecting sperm and the means (i.e., the modified MoFlo® sorter equipped with the elliptical nozzle) to achieve the result of sorting and collection rates of about 500 sorts/second.

Further, the combined references do not teach operating the high speed cell sorter at 50 psi. However, methods for sorting sperm using high speed cell sorters were well known in the art at the time the invention was made and the parameters which would effect the sorting process were also well known, including the pressure used to operate the flow cytometer. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the optimum conditions for operating the flow cytometer, and thereby to have operated the flow cytometer at at least 50 psi in order to have provided the most effective means for sorting the sperm.

Regarding step b), Seidel does not teach staining the cells with a solution of 38uM Hoechst 33342 prior to sorting the cells. However, Rens (col. 5) teaches staining the sperm with 7.1 uM Hoechst 33342 dye per  $15 \times 10^6$  sperm for 40 min at 32°C, sorting the sperm cells and then concentrating the sperm cells. It is noted that the present claims do not specify the final concentration of stain, the number of sperm or the conditions for staining the sperm. However, at the time the invention was made the

parameters which effect staining of sperm cells prior to sorting were well known in the art. Thereby, to have determined the optimum concentration of stain, depending on the quantity of sperm and the conditions (time, temp) of staining would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected the optimum concentration of stain depending on the concentration of sperm, and the conditions of staining, including to have selected the concentration of 38 uM Hoechst 33342 stain, in order to have provided the most effective means for staining the sperm to allow for accurate sorting, while maintaining the integrity and viability of the sperm.

Regarding step h), modification of the method of Seidel as set forth above would have resulted in a method in which the fertilization success level was statistically comparable to that achieved with an unsorted artificial insemination sample having about an equal number of sperm cells since the method steps would be the same and the fertilization success level is a property of the method itself. That is, since the method generated by the combined teachings of the references is the same as the claimed method, the method generated by the combined teachings necessarily achieves the

same fertilization success levels as that claimed. Additionally, in view of the teachings of Seidel regarding the importance of properly cooling sperm after sorting and during transport, performing artificial insemination soon after sorting, and selecting appropriate bulls to provide the sperm and proper artificial insemination techniques, and the teachings of Rens of how to properly handle sperm during and after the sorting process to ensure its viability, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated artificial insemination methods wherein the fertilization success level with insemination samples of less than 300,000 sorted sperm were statistically comparable to that achieved with an insemination sample comprising about an equal number of unsorted sperm. One would have been motivated to have done so in order to have achieved the benefit of generating the most effective method of artificial insemination and producing the largest possible number of bovine offspring.

Regarding claim 222, Seidel (Jan 1996) teaches the importance of inseminating bovine soon after the sorting is completed. Seidel states that insemination occurred within 9 to 29 hours of sorting and particularly exemplifies methods achieving a 50% (11 out of 22) pregnancy rate when the insemination occurred within 10 hours after sorting was completed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have inseminated the bovine with the artificial insemination sample as soon as possible following the sorting of the sample, and particularly within 5 to 9 hours following sorting, in order to have ensured the viability of the sample, thereby improving the overall effectiveness of the insemination procedure.

Regarding claim 224, in the example provided by Seidel in which a 50% (11 out of 22) pregnancy rate was achieved, the sperm were deposited deep in the uterine horn ipsilateral to the ovary with the largest follicle being determined by ultrasound. In this example, one half of the insemination sample was not inserted into each uterine horn. However, in subsequent trials, 0.05 ml (i.e., one half of the sample) was inserted into each uterine horn without ultrasonography. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have performed the artificial insemination by inserting one-half of the insemination sample into each uterine horn of the female because this would have obviated the need to use ultrasound for the insemination procedure, thereby providing a simpler and more rapid insemination procedure.

Regarding claim 225, Seidel teaches inseminating the female bovine 11 to 36 hours after the detection of estrus. Accordingly, in the method of Seidel bovine were inseminated within 11 to 26 hours after the observed standing estrus which is within the claimed range of 6 to 26 hours following observed standing estrus.

Regarding claim 227, Seidel teaches cooling and storing sperm during shipping at 5°C prior to the step of inserting.

Response to Remarks:

In the response, Applicants traversed the previous grounds of rejection under 35 USC 103. Those arguments are addressed below to the extent that they apply to the present grounds of rejection.

Applicants traversed the previous rejection by stating that the combined references do not teach the success levels claimed under the conditions recited in the claims. This argument has been fully considered but is not persuasive. The success levels achieved by the method of artificial insemination are a property of the method itself. Since the method steps resulting from the combination of the teachings of Seidel and Rens are the same as those in the claims, then the method necessarily achieves the same levels of success as that recited in the claims.

Further, as discussed in the above rejection, Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5°C during shipping were pregnant at 8 weeks. Given this 50% pregnancy rate, the method of Seidel is considered to be one that fertilizes eggs within a female bovine at success levels statistically comparable to that achieved using an artificial insemination sample comprising about the same number of unsorted sperm cells. Note that the claims do not particularly define the fertilization levels achieved using artificial insemination samples comprising about an equal number of unsorted sperm cells and that the specification has been relied upon to interpret this phrase as encompassing a 54% pregnancy rate using an insemination sample of 300,000 unsorted sperm (page 25, Example 1). Since a 50% pregnancy rate is statistically comparable to a 54% pregnancy rate (i.e., 93%), the method of Seidel which used fewer sperm than the 300,000 unsorted sperm that achieved a 54% pregnancy would necessarily have the property of achieving fertilization rates statistically comparable to that achieved using an unsorted artificial insemination sample having about an equal number of sperm cells.



Moreover, Seidel notes that pregnancy rates vary with breed of cattle, differences in the bull used to provide the sperm, insemination techniques, interval between sorting and insemination and "other factors." Thereby, there is no single success level that can be relied upon to characterize all fertilization success levels using insemination samples having an equal number of sperm cells. Given the teachings of Seidel regarding the importance of properly cooling sperm after sorting and during transport, using the sperm soon after sorting, and selecting appropriate bulls and the teachings of Rens of how to properly handle sperm during and after the sorting process to ensure its viability, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated artificial insemination methods wherein the fertilization success level with insemination samples of less than 300,000 sorted sperm were statistically comparable to that achieved with an insemination sample comprising about an equal number of unsorted sperm. One would have been motivated to have done so in order to have achieved the benefit of generating the most effective method of artificial insemination and producing bovine offspring.

Note that obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). Accordingly, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 221 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-42 of U.S. Patent Application No. 11/613,605, in view of Rens (U.S. Patent No. 5,985,216). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '605 are both drawn to methods of artificial insemination wherein the methods comprise collecting sperm cells from a male, sorting sperm cells so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The present claims and the claims of '605 are both inclusive of methods wherein the mammal is a bovine see claim 31 of '605). Further, the present claims and the claims of '605 are both inclusive of methods in which the artificial insemination sample comprises a low dosage of sperm. Note that when read in light of the specification of the '605 application, a low dosage of sperm is considered to include not more than 300,000

sperm, as is recited in the present claims. The present claims require obtaining fertilization success levels statistically comparable to that achieved with an unsorted artificial insemination sample. The claims of '605 include fertilization success levels of at least 50%, which are considered to be statistically comparable to that achieved with an unsorted insemination sample.

The claims of '605 do not recite sorting sperm cells at rates of at least 500 sorts/second.

However, Rens teaches a method of sex-sorting sperm using high speed flow cytometry. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoechst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are collected. Importantly, Rens (col. 5) discloses modifying the MoFlo® high speed cell sorter to include a new elliptical nozzle capable of more accurately orienting sperm for accurate sorting. Rens teaches use of the modified MoFlo® sorter using sampling rates of 500 sperm/second and 2000 sperm/second (column 6). Further, Rens teaches that the modified MoFlo® sorter also allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens (col. 2) teaches that the flow cytometry apparatus disclosed therein provides for improved accuracy and efficiency of sorting, as compared to prior art flow cytometers. Rens (col. 2) also discloses the

motivation to use high speed cell sorters to maximize the number of sorted sperm per unit time. For example, Rens (col. 4) discuss the requirement to use large quantities of sperm for artificial insemination and states that by using the high speed cell sorter equipped with the nozzle disclosed therein, the yield of sex sorted sperm cells can be increased at least 10 fold, making artificial insemination with sexed semen a more feasible option. Rens (col. 7) also exemplifies a method wherein a total of 50 million X and Y sperm were sorted in a 7 hour period using the modified MoFlo® sorter equipped with the new elliptical nozzle.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method claimed in '605 so as to have used high sorting rates, including sorting rates of at least 500 sorts /second, in order to have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Further, It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also *Merck & Co. v. Biocraft Labs. Inc.*, 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). In the present situation, the prior art teaches

provides the motivation to increase sort speeds to at least 500 sorts/sec and the means for achieving this result (i.e., the modified MoFlo® high speed sorter including the elliptical nozzle of Rens). Thereby, modification of the method of Seidel to use the high speed sorter of Rens to sex-sort sperm cells at rates of 500 sorts/sec would have been obvious to one of ordinary skill in the art and well within the skill of the art at the time the invention was made.

Further, the claims of '605 do not recite operating the high speed cell sorter at 50 psi. However, methods for sorting sperm using high speed cell sorters were well known in the art at the time the invention was made and the parameters which would effect the sorting process were also well known, including the pressure used to operate the flow cytometer. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the optimum conditions for operating the flow cytometer, and thereby to have operated the flow cytometer at at least 50 psi in order to have provided the most effective means for sorting the sperm.

Regarding step b), the claims of '605 recite staining the sperm with Hoechst 33342, but do not state the concentration of the Hoechst 33342. However, Rens (col. 5) teaches staining the sperm with 7.1 uM Hoechst 33342 dye per  $15 \times 10^6$  sperm for 40

min at 32°C, sorting the sperm cells and then concentrating the sperm cells. It is noted that the present claims do not specify the final concentration of stain, the number of sperm or the conditions for staining the sperm. At the time the invention was made the parameters which effect staining of sperm cells prior to sorting were well known in the art. Thereby, to have determined the optimum concentration of stain, depending on the quantity of sperm and the conditions (time, temp) of staining would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected the optimum concentration of stain depending on the concentration of sperm, and the conditions of staining, including to have selected the concentration of 38 uM Hoechst 33342 stain, in order to have provided the most effective means for staining the sperm to allow for accurate sorting, while maintaining the integrity and viability of the sperm.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 222, 224, 225 and 227 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-42

of U.S. Patent Application No. 11/613,605, in view of Rens (U.S. Patent No. 5,985,216) and further in view of Seidel (Jan 1996).

Regarding present claim 222, the claims of '605 do not recite inserting the artificial insemination sample within 5 to 9 hours after the sorting of the sperm.

However, Seidel teaches methods of bovine artificial insemination comprising collecting sperm cells from a male bovine, sorting the sperm cells according to sex using flow cytometry wherein the sperm cells are sorted at a rate of up to  $2 \times 10^6$  of each sex of sperm/5-6 hours to purity rates of about 90%, concentrating the sorted sperm cells, establishing an artificial insemination sample consisting of  $1-2 \times 10^5$  of sorted sperm cells (i.e., "no more than 300,000" sorted sperm cells) in a .1ml volume, inserting the artificial insemination sample into the uterine horns of the female bovine after the onset of estrus; and fertilizing at least one egg within said female bovine. Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5°C during shipping were pregnant at 8 weeks.

Seidel also teaches the importance of inseminating bovine soon after the sorting is completed. Seidel states that insemination occurred within 9 to 29 hours of sorting and particularly exemplifies methods achieving a 50% (11 out of 22) pregnancy rate when the insemination occurred within 10 hours after sorting was completed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have inseminated the bovine with the artificial insemination sample as soon as possible following the sorting of the sample, and particularly within 5

to 9 hours following sorting, in order to have ensured the viability of the sample, thereby improving the overall effectiveness of the insemination procedure.

Regarding present claim 224, the claims of '605 do not recite inserting one-half of the insemination sample into each uterine horn. However, Seidel exemplifies methods wherein a 50% (11 out of 22) pregnancy rate was achieved, and wherein the sperm were deposited deep in the uterine horn ipsilateral to the ovary with the largest follicle being determined by ultrasound. Seidel also teaches that, in subsequent trials, 0.05 ml (i.e., one half of the sample) was inserted into each uterine horn without ultrasonography. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods claimed in '605 so as to have performed the artificial insemination by inserting one-half of the insemination sample into each uterine horn of the female because this would have obviated the need to use ultrasound for the insemination procedure, thereby providing a simpler and more rapid insemination procedure.

Regarding present claim 225, the claims of '605 do not recite inseminating the female bovine 11 to 26 hours after estrus. However, Seidel teaches inseminating the female bovine 11 to 36 hours after the detection of estrus. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method claimed in '605 so as to have inseminated the bovine soon after the onset of estrus, and particularly within 11 to 26 hours after the observed standing estrus, in order to enhance the effectiveness of the artificial insemination method.



Art Unit: 1634

Regarding present claim 227, the claims of '605 do not recite cooling the sperm to 5°C. However, Seidel (Jan 1996) teaches sorting sperm and storing sperm during shipping at 5°C. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method claimed in '605 so that when sperm was to be shipped, cooling the sperm to 5°C during shipping, in order to have ensured the viability of the sperm, thereby improving the effectiveness of the artificial insemination method.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Carla Myers/  
Primary Examiner, Art Unit 1634